Clinical trial results:
A 12-week, multicenter, randomized, double-blind, parallel-arm, placebo-controlled study to assess the efficacy and safety of CSJ117, when added to existing asthma therapy in patients 18 years of age with severe uncontrolled asthma

Summary

EudraCT number	2019-004905-29
Trial protocol	DE CZ LV HU BE PL BG FR SK IT ES
Global end of trial date	06 September 2022

Results information

Result version number	v1 (current)
This version publication date	03 August 2023
First version publication date	03 August 2023

Trial information

Trial identification

Sponsor protocol code	CCSJ117A12201C

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04410523
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 September 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 September 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial was to characterize the dose-response relationship of five doses of CSJ117 inhaled daily on lung function, compared with placebo, at the end of the 12-week active-treatment period.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 September 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Philippines: 7
Country: Number of subjects enrolled	Russian Federation: 8
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Bulgaria: 13
Country: Number of subjects enrolled	Czechia: 10
Country: Number of subjects enrolled	Germany: 50
Country: Number of subjects enrolled	Hungary: 17
Country: Number of subjects enrolled	Latvia: 14
Country: Number of subjects enrolled	Poland: 29
Country: Number of subjects enrolled	Slovakia: 2
Country: Number of subjects enrolled	Japan: 64
Country: Number of subjects enrolled	Argentina: 53
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Guatemala: 12
Country: Number of subjects enrolled	United States: 47
Worldwide total number of subjects	335
EEA total number of subjects	138

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	281
From 65 to 84 years	54
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in 116 investigative sites in 15 countries.

Pre-assignment

Screening details:

The screening period of approximately 2 weeks began after the participants had provided written informed consent. There was a single blinded placebo run-in period of 4 weeks (extended to 8 weeks in case of asthma exacerbation or respiratory tract infection during the run-in period) before starting the double blinded treatment period.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	CSJ117 0.5mg

Arm description:

CSJ117 0.5 mg inhaled once daily

Arm type	Experimental
Investigational medicinal product name	CSJ117
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Run-in period: Placebo inhaled once daily (in the morning) for 4 weeks. Placebo dosing extended to 8 weeks in case of asthma exacerbation or respiratory tract infection during this period.
Treatment period: CSJ117 0.5 mg inhaled once daily (in the morning) for 12 weeks. Delivered via Concept1 device.

Arm title	CSJ117 1mg

Arm description:

CSJ117 1 mg inhaled once daily

Arm type	Experimental
Investigational medicinal product name	CSJ117
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Run-in period: Placebo inhaled once daily (in the morning) for 4 weeks. Placebo dosing extended to 8 weeks in case of asthma exacerbation or respiratory tract infection during this period.
Treatment period: CSJ117 1 mg inhaled once daily (in the morning) for 12 weeks. Delivered via Concept1 device.

Arm title	CSJ117 2mg

Arm description:

CSJ117 2 mg inhaled once daily

Arm type	Experimental

Investigational medicinal product name	CSJ117
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Run-in period: Placebo inhaled once daily (in the morning) for 4 weeks. Placebo dosing extended to 8 weeks in case of asthma exacerbation or respiratory tract infection during this period.
Treatment period: CSJ117 2 mg inhaled once daily (in the morning) for 12 weeks. Delivered via Concept1 device.

Arm title	CSJ117 4mg

Arm description:

CSJ117 4 mg inhaled once daily

Arm type	Experimental
Investigational medicinal product name	CSJ117
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Run-in period: Placebo inhaled once daily (in the morning) for 4 weeks. Placebo dosing extended to 8 weeks in case of asthma exacerbation or respiratory tract infection during this period.
Treatment period: CSJ117 4 mg inhaled once daily (in the morning) for 12 weeks. Delivered via Concept1 device.

Arm title	CSJ117 8mg

Arm description:

CSJ117 8 mg inhaled once daily

Arm type	Experimental
Investigational medicinal product name	CSJ117
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Run-in period: Placebo inhaled once daily (in the morning) for 4 weeks. Placebo dosing extended to 8 weeks in case of asthma exacerbation or respiratory tract infection during this period.
Treatment period: CSJ117 8 mg inhaled once daily (in the morning) for 12 weeks. Delivered via Concept1 device.

Arm title	Placebo

Arm description:

Placebo inhaled once daily

Arm type	Placebo
Investigational medicinal product name	CSJ117
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Run-in period: Placebo inhaled once daily (in the morning) for 4 weeks. Placebo dosing extended to 8 weeks in case of asthma exacerbation or respiratory tract infection during this period.
Treatment period: Placebo inhaled once daily (in the morning) for 12 weeks. Delivered via Concept1 device.

Number of subjects in period 1	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg
Started	36	37	37
Completed	32	32	35
Not completed	4	5	2
Physician decision	-	1	-
Adverse Event	1	-	-
Subject decision	2	-	-
Protocol deviation	-	-	-
Pregnancy	-	-	-
Study terminated by sponsor	1	3	2
Lost to follow-up	-	1	-

Number of subjects in period 1	CSJ117 4mg	CSJ117 8mg	Placebo
Started	76	74	75
Completed	69	71	65
Not completed	7	3	10
Physician decision	-	-	-
Adverse Event	-	-	2
Subject decision	1	-	1
Protocol deviation	-	-	2
Pregnancy	-	-	1
Study terminated by sponsor	6	3	4
Lost to follow-up	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	CSJ117 0.5mg
Reporting group description: CSJ117 0.5 mg inhaled once daily	
Reporting group title	CSJ117 1mg
Reporting group description: CSJ117 1 mg inhaled once daily	
Reporting group title	CSJ117 2mg
Reporting group description: CSJ117 2 mg inhaled once daily	
Reporting group title	CSJ117 4mg
Reporting group description: CSJ117 4 mg inhaled once daily	
Reporting group title	CSJ117 8mg
Reporting group description: CSJ117 8 mg inhaled once daily	
Reporting group title	Placebo
Reporting group description: Placebo inhaled once daily	

Reporting group values	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg
Number of subjects	36	37	37
Age Categorical Units: participants			
18 - <40 years	9	6	8
40 - <65 years	23	26	23
≥65 years	4	5	6
Age Continuous Units: years			
arithmetic mean	49.8	51.2	51.4
standard deviation	± 12.89	± 12.09	± 13.31
Sex: Female, Male Units: participants			
Female	27	25	21
Male	9	12	16
Race/Ethnicity, Customized Units: Subjects			
Asian	8	8	7
American Indian or Alaska Native	1	3	0
Black or African American	1	0	0
White	26	26	30

Reporting group values	CSJ117 4mg	CSJ117 8mg	Placebo
Number of subjects	76	74	75

Age Categorical Units: participants			
18 - <40 years	16	10	19
40 - <65 years	50	50	41
≥65 years	10	14	15
Age Continuous Units: years			
arithmetic mean	50.3	52.7	51.5
standard deviation	± 12.80	± 12.22	± 13.46
Sex: Female, Male Units: participants			
Female	43	48	45
Male	33	26	30
Race/Ethnicity, Customized Units: Subjects			
Asian	17	16	17
American Indian or Alaska Native	1	1	3
Black or African American	2	5	2
White	56	52	53

Reporting group values	Total		
Number of subjects	335		
Age Categorical Units: participants			
18 - <40 years	68		
40 - <65 years	213		
≥65 years	54		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: participants			
Female	209		
Male	126		
Race/Ethnicity, Customized Units: Subjects			
Asian	73		
American Indian or Alaska Native	9		
Black or African American	10		
White	243		

End points

End points reporting groups

Reporting group title	CSJ117 0.5mg
Reporting group description: CSJ117 0.5 mg inhaled once daily	
Reporting group title	CSJ117 1mg
Reporting group description: CSJ117 1 mg inhaled once daily	
Reporting group title	CSJ117 2mg
Reporting group description: CSJ117 2 mg inhaled once daily	
Reporting group title	CSJ117 4mg
Reporting group description: CSJ117 4 mg inhaled once daily	
Reporting group title	CSJ117 8mg
Reporting group description: CSJ117 8 mg inhaled once daily	
Reporting group title	Placebo
Reporting group description: Placebo inhaled once daily	

Primary: Average change from baseline in pre-dose FEV1 at Week 8 and Week 12

End point title	Average change from baseline in pre-dose FEV1 at Week 8 and Week 12

End point description:

FEV1 (forced expiratory volume in one second) is the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation, measured through spirometry testing.
Pre-dose FEV1 is defined as average of the two FEV1 measurements taken at approximately 45 minutes and 15 minutes prior to dosing.
The baseline pre-dose FEV1 value is defined as the average of the values taken approximately 2 hours 45 minutes and 2 hours 15 minutes prior to the first dose of double-blind treatment at Day 1.
The least-squares means for change from baseline in pre-dose FEV1 averaged between Week 8 and Week 12 visits for each individual dose group were obtained from a linear mixed effects model for repeated measures (MMRM).
A positive average change from baseline in pre-dose FEV1 is considered a favorable outcome.

End point type	Primary
End point timeframe: Baseline, Weeks 8-12	

End point values	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	37	37	76
Units: liters (L)				
least squares mean (standard error)	0.173 (± 0.0445)	0.109 (± 0.0446)	0.116 (± 0.0419)	0.060 (± 0.0299)

End point values	CSJ117 8mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	75		
Units: liters (L)				
least squares mean (standard error)	0.043 (± 0.0305)	0.051 (± 0.0309)		

Statistical analyses

Statistical analysis title	pre-dose FEV1
Statistical analysis description: Treatment difference (CSJ117-placebo)	
Comparison groups	CSJ117 1mg v Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.286
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	0.058
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.049
upper limit	0.165
Variability estimate	Standard error of the mean
Dispersion value	0.0542

Statistical analysis title	pre-dose FEV1
Statistical analysis description: Treatment difference (CSJ117-placebo)	
Comparison groups	CSJ117 0.5mg v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.025
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	0.122

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.016
upper limit	0.229
Variability estimate	Standard error of the mean
Dispersion value	0.0541

Statistical analysis title	pre-dose FEV1
Statistical analysis description: Treatment difference (CSJ117-placebo)	
Comparison groups	CSJ117 4mg v Placebo
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.831
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	0.009
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.076
upper limit	0.094
Variability estimate	Standard error of the mean
Dispersion value	0.043

Statistical analysis title	pre-dose FEV1
Statistical analysis description: Treatment difference (CSJ117-placebo)	
Comparison groups	CSJ117 8mg v Placebo
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.852
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	-0.008
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.094
upper limit	0.077
Variability estimate	Standard error of the mean
Dispersion value	0.0434

Statistical analysis title	pre-dose FEV1
Statistical analysis description: Treatment difference (CSJ117-placebo)	
Comparison groups	CSJ117 2mg v Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.212
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	0.065
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.037
upper limit	0.168
Variability estimate	Standard error of the mean
Dispersion value	0.0521

Secondary: Average change from baseline in FeNO at Week 8 and Week 12

End point title	Average change from baseline in FeNO at Week 8 and Week 12

End point description:

Fractional exhaled Nitric Oxide (FeNO) pre-dose measurements were done at the investigational sites prior to spirometry assessments. FeNO is defined as the mean of two serial measurements. The measurement of exhaled nitric oxide is widely accepted as a non-invasive marker of airway inflammation (inflammation leads to elevation of FeNO).
The baseline FeNO pre-dose measurements were taken at the end of the run-in period.
The least-squares means for change from baseline in FeNO averaged between Week 8 and Week 12 visits for each individual dose group were obtained from a linear mixed effects model for repeated measures (MMRM).
A negative average change from baseline in FeNO is considered a favorable outcome.

End point type	Secondary

End point timeframe:

Baseline, Weeks 8-12

End point values	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	37	37	76
Units: parts per billion (ppb)				
least squares mean (standard error)	-2.869 (± 1.9670)	-5.299 (± 1.9872)	-4.190 (± 1.8760)	-1.587 (± 1.3312)

End point values	CSJ117 8mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	75		
Units: parts per billion (ppb)				
least squares mean (standard error)	-0.208 (± 1.3248)	-1.301 (± 1.3142)		

Statistical analyses

Statistical analysis title	FeNO
Statistical analysis description: Treatment difference (CSJ117-placebo)	
Comparison groups	CSJ117 0.5mg v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.508
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	-1.568
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.219
upper limit	3.083
Variability estimate	Standard error of the mean
Dispersion value	2.363

Statistical analysis title	FeNO
Statistical analysis description: Treatment difference (CSJ117-placebo)	
Comparison groups	CSJ117 1mg v Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.095
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	-3.998
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.691
upper limit	0.695
Variability estimate	Standard error of the mean
Dispersion value	2.384

Statistical analysis title	FeNO
Statistical analysis description: Treatment difference (CSJ117-placebo)	
Comparison groups	CSJ117 2mg v Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.209
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	-2.889
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.405
upper limit	1.627
Variability estimate	Standard error of the mean
Dispersion value	2.2943

Statistical analysis title	FeNO
Statistical analysis description: Treatment difference (CSJ117-placebo)	
Comparison groups	CSJ117 4mg v Placebo
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.878
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	-0.287
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.971
upper limit	3.398
Variability estimate	Standard error of the mean
Dispersion value	1.8718

Statistical analysis title	FeNO
Statistical analysis description: Treatment difference (CSJ117-placebo)	
Comparison groups	CSJ117 8mg v Placebo

Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.558
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	1.093
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.578
upper limit	4.765
Variability estimate	Standard error of the mean
Dispersion value	1.8652

Secondary: Change from baseline in morning PEF at Week 12

End point title	Change from baseline in morning PEF at Week 12

End point description:

PEF (Peak Expiratory Flow) is a person's maximum speed of expiration. All participants were instructed to record PEF twice daily before taking any medication using an electronic peak expiratory flow device (eDiary/ePEF), once in the morning and once approximately 12 hours later in the evening at home. At each timepoint, the participant was instructed to perform 3 consecutive manoeuvres within 10 minutes. These PEF values were captured in the eDiary/ePEF.
Mean morning and evening PEF values were calculated by weekly intervals.
The baseline values of PEF were the mean values in the run-in period.
A positive change from baseline in PEF is considered a favorable outcome.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	33	32	65
Units: liters/minute				
arithmetic mean (standard deviation)	-0.9785 (± 22.73169)	-1.7035 (± 28.83957)	18.9496 (± 50.09045)	-0.0319 (± 33.56218)

End point values	CSJ117 8mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	61		
Units: liters/minute				
arithmetic mean (standard deviation)	3.5702 (± 37.05293)	-2.2060 (± 24.56187)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in evening PEF at Week 12

End point title	Change from baseline in evening PEF at Week 12

End point description:

PEF (Peak Expiratory Flow) is a person's maximum speed of expiration. All participants were instructed to record PEF twice daily before taking any medication using an electronic peak expiratory flow device (eDiary/ePEF), once in the morning and once approximately 12 hours later in the evening at home. At each timepoint, the participant was instructed to perform 3 consecutive manoeuvres within 10 minutes. These PEF values were captured in the eDiary/ePEF.
Mean morning and evening PEF values were calculated by weekly intervals.
The baseline values of PEF were the mean values in the run-in period.
A positive change from baseline in PEF is considered a favorable outcome.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	30	31	59
Units: liters/minute				
arithmetic mean (standard deviation)	-5.3894 (± 29.13968)	-7.8709 (± 29.06055)	14.0265 (± 44.90062)	0.3893 (± 30.47064)

End point values	CSJ117 8mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	58		
Units: liters/minute				
arithmetic mean (standard deviation)	2.6905 (± 32.27860)	-3.2785 (± 22.93816)		

Statistical analyses

No statistical analyses for this end point

Secondary: Average change from baseline in ACQ-5 score at Week 8 and Week 12

End point title	Average change from baseline in ACQ-5 score at Week 8 and

	Week 12

End point description:

The Asthma Control Questionnaire-5 (ACQ-5) is a five-item, self-completed questionnaire, which is used as a measure of asthma symptom control. Patients were asked to recall how their asthma had been during the previous week and to respond to the symptom questions on a 7-point scale (0=no impairment, 6=maximum impairment). The questions are equally weighted and the overall ACQ-5 score is the mean of all 5 questions, therefore between 0 (totally controlled) and 6 (severely uncontrolled).
The baseline values of ACQ-5 were collected at the end of the run-in period.
The least-squares means for change from baseline in ACQ-5 score averaged between Week 8 and Week 12 visits for each individual dose group were obtained from a linear mixed effects model for repeated measures (MMRM).
A negative change from baseline in ACQ-5 is considered a favorable outcome.

End point type	Secondary

End point timeframe:

Baseline, Weeks 8-12

End point values	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	37	37	76
Units: score on a scale				
least squares mean (standard error)	-0.764 (± 0.1230)	-1.142 (± 0.1225)	-1.011 (± 0.1171)	-0.739 (± 0.0824)

End point values	CSJ117 8mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	75		
Units: score on a scale				
least squares mean (standard error)	-0.837 (± 0.0829)	-0.722 (± 0.0846)		

Statistical analyses

Statistical analysis title	ACQ-5

Statistical analysis description:

Treatment difference (CSJ117-placebo)

Comparison groups	CSJ117 0.5mg v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.78
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	-0.042

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.336
upper limit	0.252
Variability estimate	Standard error of the mean
Dispersion value	0.1493

Statistical analysis title	ACQ-5
Statistical analysis description: Treatment difference (CSJ117-placebo)	
Comparison groups	CSJ117 1mg v Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	-0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.713
upper limit	-0.127
Variability estimate	Standard error of the mean
Dispersion value	0.1489

Statistical analysis title	ACQ-5
Statistical analysis description: Treatment difference (CSJ117-placebo)	
Comparison groups	CSJ117 8mg v Placebo
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.333
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	-0.115
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.348
upper limit	0.118
Variability estimate	Standard error of the mean
Dispersion value	0.1184

Statistical analysis title	ACQ-5
Statistical analysis description: Treatment difference (CSJ117-placebo)	
Comparison groups	CSJ117 4mg v Placebo
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.887
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	-0.017
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.249
upper limit	0.216
Variability estimate	Standard error of the mean
Dispersion value	0.1182

Statistical analysis title	ACQ-5
Statistical analysis description: Treatment difference (CSJ117-placebo)	
Comparison groups	CSJ117 2mg v Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.047
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	-0.289
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.573
upper limit	0.004
Variability estimate	Standard error of the mean
Dispersion value	0.1446

Secondary: Average change from baseline in AQLQ+12 score at Week 8 and Week 12

End point title	Average change from baseline in AQLQ+12 score at Week 8 and Week 12

End point description:

The Asthma Quality of Life Questionnaire+12 (AQLQ+12) is a disease specific questionnaire, which is used as a measure of health-related quality of life. The AQLQ+12 comprises a total of 32 individual questions that span a total of 4 domains: symptoms, activity limitation, emotional function, and environmental stimuli. Patients are asked to recall their experiences during the previous 2 weeks and to score each item on a 7-point scale (7 = not at all impaired to 1 = severely impaired). The overall AQLQ+12 score is the mean of all 32 individual responses, therefore between 7 and 1 with higher scores indicating less impairment in health-related quality of life.
The baseline values of AQLQ+12 were collected at the end of the run-in period.
The least-squares means for change from baseline in AQLQ+12 score averaged between Week 8 and Week 12 visits were obtained from a linear mixed effects model for repeated measures (MMRM).
A positive change from baseline is considered a favorable outcome.

End point type	Secondary

End point timeframe:

Baseline, Weeks 8-12

End point values	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	37	37	76
Units: score on a scale				
least squares mean (standard error)	0.467 (± 0.1223)	0.781 (± 0.1220)	0.642 (± 0.1177)	0.597 (± 0.0828)

End point values	CSJ117 8mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	75		
Units: score on a scale				
least squares mean (standard error)	0.636 (± 0.0826)	0.564 (± 0.0842)		

Statistical analyses

Statistical analysis title	AQLQ+12

Statistical analysis description:

Treatment difference (CSJ117-placebo)

Comparison groups	CSJ117 0.5mg v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.515
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	-0.097

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.389
upper limit	0.195
Variability estimate	Standard error of the mean
Dispersion value	0.1485

Statistical analysis title	AQLQ+12
Statistical analysis description: Treatment difference (CSJ117-placebo)	
Comparison groups	CSJ117 1mg v Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.143
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	0.218
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.074
upper limit	0.51
Variability estimate	Standard error of the mean
Dispersion value	0.1484

Statistical analysis title	AQLQ+12
Statistical analysis description: Treatment difference (CSJ117-placebo)	
Comparison groups	CSJ117 4mg v Placebo
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.778
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	0.033
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.199
upper limit	0.265
Variability estimate	Standard error of the mean
Dispersion value	0.118

Statistical analysis title	AQLQ+12
Statistical analysis description: Treatment difference (CSJ117-placebo)	
Comparison groups	CSJ117 8mg v Placebo
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.539
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	0.073
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.305
Variability estimate	Standard error of the mean
Dispersion value	0.118

Statistical analysis title	AQLQ+12
Statistical analysis description: Treatment difference (CSJ117-placebo)	
Comparison groups	CSJ117 2mg v Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.59
Method	MMRM
Parameter estimate	Least Squares mean
Point estimate	0.078
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.207
upper limit	0.364
Variability estimate	Standard error of the mean
Dispersion value	0.145

Secondary: Change from baseline in ADSD score at Week 8 and Week 12

End point title	Change from baseline in ADSD score at Week 8 and Week 12

End point description:

Asthma Daytime Symptom Diary (ADSD) and Asthma Nighttime Symptom Diary (ANSD) are patient reported outcome measures of asthma symptom severity.

Patients recorded asthma symptoms twice daily in the eDiary. Severity of daytime asthma symptoms were assessed before going to bed and severity of nighttime symptoms upon waking.
Both diaries comprised of 6 items assessing breathing symptoms (difficulty breathing, wheezing, and shortness of breath), chest symptoms (chest tightness and chest pain), and cough symptoms (cough). All items were assessed using an 11-point numeric rating scale ranging from 0 ('None') to 10 ('As bad as you can imagine'). The overall score is the mean of all 6 individual responses, therefore between 0 and 10 with higher scores indicating more severe symptoms.
Mean daily scores of both diaries were calculated by weekly intervals. The baseline values were defined as the average score during the run-in period.
A negative change from baseline is a favorable outcome.

End point type	Secondary

End point timeframe:

Baseline, Week 8 and Week 12

End point values	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	33	37	73
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 8 (n=33,33,37,73,72,67)	-0.24 (± 0.678)	-0.42 (± 0.622)	-0.35 (± 0.773)	-0.32 (± 0.555)
Week 12 (n=32,32,32,68,65,64)	-0.29 (± 0.752)	-0.59 (± 0.938)	-0.38 (± 0.687)	-0.33 (± 0.581)

End point values	CSJ117 8mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	67		
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 8 (n=33,33,37,73,72,67)	-0.33 (± 0.787)	-0.25 (± 0.580)		
Week 12 (n=32,32,32,68,65,64)	-0.35 (± 0.820)	-0.37 (± 0.754)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in ANSD score at Week 8 and Week 12

End point title	Change from baseline in ANSD score at Week 8 and Week 12

End point description:

Asthma Daytime Symptom Diary (ADSD) and Asthma Nighttime Symptom Diary (ANSD) are patient reported outcome measures of asthma symptom severity.
Patients recorded asthma symptoms twice daily in the eDiary. Severity of daytime asthma symptoms were assessed before going to bed and severity of nighttime symptoms upon waking.
Both diaries comprised of 6 items assessing breathing symptoms (difficulty breathing, wheezing, and shortness of breath), chest symptoms (chest tightness and chest pain), and cough symptoms (cough). All items were assessed using an 11-point numeric rating scale ranging from 0 ('None') to 10 ('As bad as you can imagine'). The overall score is the mean of all 6 individual responses, therefore between 0 and

10 with higher scores indicating more severe symptoms.
Mean daily scores of both diaries were calculated by weekly intervals. The baseline values were defined as the average score during the run-in period.
A negative change from baseline is a favorable outcome.

End point type	Secondary

End point timeframe:

Baseline, Week 8 and Week 12

End point values	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	34	37	74
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 8 (n=33,34,37,74,72,69)	-0.15 (± 0.637)	-0.35 (± 0.629)	-0.30 (± 0.760)	-0.27 (± 0.547)
Week 12 (n=34,33,35,70,69,66)	-0.19 (± 0.480)	-0.46 (± 0.868)	-0.29 (± 0.695)	-0.26 (± 0.590)

End point values	CSJ117 8mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	69		
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 8 (n=33,34,37,74,72,69)	-0.26 (± 0.753)	-0.25 (± 0.634)		
Week 12 (n=34,33,35,70,69,66)	-0.23 (± 0.769)	-0.33 (± 0.729)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in number of puffs of SABA taken per day at Week 12

End point title	Change from baseline in number of puffs of SABA taken per day at Week 12

End point description:

Participants were given a short acting β2-agonist (SABA) such as salbutamol (100 µg) or albuterol (90 µg) to use as rescue medication throughout the study. Participants recorded in the eDiary, once in the morning and once in the evening, the use of rescue medication (number of puffs of SABA taken in the previous 12 hours). The total number of puffs of SABA taken per day was calculated and the mean daily use of puffs of SABA was derived by weekly intervals.
The baseline value of number of puffs of SABA taken per day is the average of total daily SABA use during the run-in period.
A negative change from baseline is considered a favorable outcome.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	33	35	70
Units: puffs of SABA per day				
arithmetic mean (standard deviation)	-0.2189 (± 0.72340)	-0.4548 (± 0.88125)	-0.3420 (± 0.68267)	-0.4310 (± 0.80279)

End point values	CSJ117 8mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	68		
Units: puffs of SABA per day				
arithmetic mean (standard deviation)	-0.3766 (± 0.98070)	-0.3543 (± 0.78420)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with on-treatment adverse events (AEs) and serious adverse events (SAEs) during the on-treatment period

End point title	Number of participants with on-treatment adverse events (AEs) and serious adverse events (SAEs) during the on-treatment period

End point description:

Number of participants with AEs and SAEs, including asthma exacerbations, changes from baseline in vital signs, electrocardiograms and laboratory results qualifying and reported as AEs during the on-treatment period.
The on-treatment period is between the date of first dose of double-blind study treatment and date of the last dose of randomized study treatment.
Grades to characterize the severity of the adverse events were based on the Common Terminology Criteria for Adverse Events (CTCAE). For CTCAE, Grade 1 = mild; Grade 2 = moderate; Grade 3 = severe; Grade 4 = life-threatening; Grade 5 = death related to AE.
The number of participants in each category is reported in the table.

End point type	Secondary

End point timeframe:

From first dose of double-blind study treatment up to last dose (Week 12)

End point values	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	37	37	76
Units: participants				
At least one AE	12	10	13	22
Mild AEs	5	8	6	9
Moderate AEs	6	2	7	12
Severe AEs	1	0	0	1
Study treatment-related AEs	0	1	1	2
SAEs	1	0	0	0
AEs leading to discontinuation	1	0	0	0

End point values	CSJ117 8mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	75		
Units: participants				
At least one AE	25	23		
Mild AEs	13	13		
Moderate AEs	12	10		
Severe AEs	0	0		
Study treatment-related AEs	4	2		
SAEs	0	1		
AEs leading to discontinuation	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with anti-CSJ117 antibodies

End point title	Number of participants with anti-CSJ117 antibodies

End point description:

Immunogenicity (antibody formation against CSJ117) was evaluated in serum by a validated bridging electrochemiluminescence immunoassay (ECLIA).

End point type	Secondary

End point timeframe:

Day 1 and Weeks 2, 4, 8, 12, 14, 16, 20 and 24

End point values	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	36	37	76
Units: participants				
Day 1 : Negative (n=36,36,37,76,74,75)	30	33	31	66

Day 1 : Positive (n=36,36,37,76,74,75)	6	3	6	10
Week 2 : Negative (n=35,35,37,75,74,69)	27	31	31	65
Week 2 : Positive (n=35,35,37,75,74,69)	8	4	6	10
Week 4 : Negative (n=33,35,37,74,71,71)	26	29	26	49
Week 4 : Positive (n=33,35,37,74,71,71)	7	6	11	25
Week 8 : Negative (n=34,33,37,72,72,67)	17	16	10	22
Week 8 : Positive (n=34,33,37,72,72,67)	17	17	27	50
Week 12 : Negative (n=33,33,35,71,71,66)	9	11	5	19
Week 12 : Positive (n=33,33,35,71,71,66)	24	22	30	52
Week 14 : Negative (n=26,25,29,59,52,56)	7	6	3	13
Week 14 : Positive (n=26,25,29,59,52,56)	19	19	26	46
Week 16 : Negative (n=26,25,29,58,53,56)	7	8	3	12
Week 16 : Positive (n=26,25,29,58,53,56)	19	17	26	46
Week 20 : Negative (n=26,25,29,58,53,55)	9	9	6	13
Week 20 : Positive (n=26,25,29,58,53,55)	17	16	23	45
Week 24 : Negative (n=26,25,28,56,53,56)	11	10	5	13
Week 24 : Positive (n=26,25,28,56,53,56)	15	15	23	43

End point values	CSJ117 8mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	75		
Units: participants				
Day 1 : Negative (n=36,36,37,76,74,75)	63	63		
Day 1 : Positive (n=36,36,37,76,74,75)	11	12		
Week 2 : Negative (n=35,35,37,75,74,69)	64	56		
Week 2 : Positive (n=35,35,37,75,74,69)	10	13		
Week 4 : Negative (n=33,35,37,74,71,71)	47	57		
Week 4 : Positive (n=33,35,37,74,71,71)	24	14		
Week 8 : Negative (n=34,33,37,72,72,67)	18	58		
Week 8 : Positive (n=34,33,37,72,72,67)	54	9		
Week 12 : Negative (n=33,33,35,71,71,66)	11	53		
Week 12 : Positive (n=33,33,35,71,71,66)	60	13		

Week 14 : Negative (n=26,25,29,59,52,56)	6	49		
Week 14 : Positive (n=26,25,29,59,52,56)	46	7		
Week 16 : Negative (n=26,25,29,58,53,56)	7	49		
Week 16 : Positive (n=26,25,29,58,53,56)	46	7		
Week 20 : Negative (n=26,25,29,58,53,55)	6	47		
Week 20 : Positive (n=26,25,29,58,53,55)	47	8		
Week 24 : Negative (n=26,25,28,56,53,56)	8	49		
Week 24 : Positive (n=26,25,28,56,53,56)	45	7		

Statistical analyses

No statistical analyses for this end point

Secondary: CSJ117 serum concentration

End point title	CSJ117 serum concentration[1]

End point description:

CSJ117 concentration was determined in serum by a validated immunoassay method. Concentrations below the lower limit of quantification (LLOQ) were treated as "zero".

End point type	Secondary

End point timeframe:

Day 1 and Week 12: pre-dose, 2 and 4 hours post-dose; Weeks 2, 4 and 8: pre-dose and 4 hours post-dose; Weeks 14, 16, 20 and 24: pre-dose

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is not applicable to placebo

End point values	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	37	37	75
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 1, pre-dose (n=36,37,36,74,73)	0.00 (± 0.00)	0.00 (± 0.00)	1.34 (± 8.02)	0.00 (± 0.00)
Day 1, 2 hours post-dose (n=36,37,37,74,74)	0.00 (± 0.00)	0.00 (± 0.00)	1.86 (± 7.36)	0.00 (± 0.00)
Day 1, 4 hours post-dose (n=36,37,37,74,73)	0.00 (± 0.00)	0.00 (± 0.00)	1.97 (± 7.90)	0.214 (± 1.33)
Week 2, pre-dose (n=35,35,37,75,74)	0.320 (± 1.89)	0.00 (± 0.00)	2.32 (± 8.57)	2.00 (± 4.74)
Week 2, 2 hours post-dose (n=36,34,37,73,74)	0.389 (± 2.30)	0.00 (± 0.00)	2.20 (± 8.05)	1.66 (± 3.51)
Week 4, pre-dose (n=33,35,36,74,70)	0.336 (± 1.93)	0.00 (± 0.00)	2.89 (± 9.03)	2.86 (± 5.11)
Week 4, 2 hours post-dose (n=33,34,37,74,69)	0.467 (± 2.68)	0.00 (± 0.00)	3.19 (± 9.01)	3.59 (± 5.69)
Week 8, pre-dose (n=33,33,37,72,71)	1.69 (± 4.34)	3.15 (± 6.50)	6.79 (± 12.0)	11.5 (± 15.8)
Week 8, 2 hours post-dose (n=33,33,36,71,68)	1.84 (± 4.69)	3.29 (± 6.85)	6.94 (± 12.2)	11.1 (± 14.7)

Week 12, pre-dose (n=32,33,31,69,70)	1.83 (± 4.69)	2.20 (± 4.61)	10.3 (± 16.8)	14.6 (± 20.3)
Week 12, 2 hours post-dose (n=32,32,31,68,68)	2.02 (± 4.68)	2.49 (± 4.81)	10.2 (± 16.4)	14.3 (± 20.3)
Week 12, 4 hours post-dose (n=32,32,31,68,68)	2.11 (± 4.84)	2.51 (± 4.79)	10.1 (± 16.3)	15.2 (± 20.7)
Week 14, pre-dose (n=25,25,27,58,52)	0.239 (± 1.19)	0.00 (± 0.00)	2.97 (± 10.1)	1.59 (± 4.43)
Week 16, pre-dose (n=25,25,27,57,53)	0.00 (± 0.00)	0.00 (± 0.00)	2.16 (± 10.0)	0.424 (± 1.92)
Week 20, pre-dose (n=25,25,27,58,53)	0.00 (± 0.00)	0.00 (± 0.00)	1.94 (± 8.99)	0.00 (± 0.00)
Week 24, pre-dose (n=25,25,26,55,53)	0.00 (± 0.00)	0.00 (± 0.00)	1.86 (± 6.81)	0.00 (± 0.00)

End point values	CSJ117 8mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 1, pre-dose (n=36,37,36,74,73)	0.00 (± 0.00)			
Day 1, 2 hours post-dose (n=36,37,37,74,74)	0.157 (± 0.947)			
Day 1, 4 hours post-dose (n=36,37,37,74,73)	0.924 (± 2.58)			
Week 2, pre-dose (n=35,35,37,75,74)	6.58 (± 7.61)			
Week 2, 2 hours post-dose (n=36,34,37,73,74)	7.66 (± 7.83)			
Week 4, pre-dose (n=33,35,36,74,70)	12.0 (± 19.5)			
Week 4, 2 hours post-dose (n=33,34,37,74,69)	13.8 (± 22.2)			
Week 8, pre-dose (n=33,33,37,72,71)	39.3 (± 51.0)			
Week 8, 2 hours post-dose (n=33,33,36,71,68)	39.8 (± 49.9)			
Week 12, pre-dose (n=32,33,31,69,70)	49.5 (± 62.1)			
Week 12, 2 hours post-dose (n=32,32,31,68,68)	45.7 (± 49.7)			
Week 12, 4 hours post-dose (n=32,32,31,68,68)	46.7 (± 52.2)			
Week 14, pre-dose (n=25,25,27,58,52)	7.26 (± 15.7)			
Week 16, pre-dose (n=25,25,27,57,53)	2.53 (± 8.10)			
Week 20, pre-dose (n=25,25,27,58,53)	0.163 (± 1.19)			
Week 24, pre-dose (n=25,25,26,55,53)	0.00 (± 0.00)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From first dose of double-blind study treatment up to 12 weeks after last dose (Week 24)	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0
Reporting groups	
Reporting group title	CSJ117 8mg
Reporting group description: CSJ117 8 mg inhaled once daily	
Reporting group title	CSJ117 4mg
Reporting group description: CSJ117 4 mg inhaled once daily	
Reporting group title	CSJ117 2mg
Reporting group description: CSJ117 2 mg inhaled once daily	
Reporting group title	CSJ117 1mg
Reporting group description: CSJ117 1 mg inhaled once daily	
Reporting group title	CSJ117 0.5mg
Reporting group description: CSJ117 0.5 mg inhaled once daily	
Reporting group title	Placebo
Reporting group description: Placebo inhaled once daily	

Serious adverse events	CSJ117 8mg	CSJ117 4mg	CSJ117 2mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 74 (0.00%)	1 / 76 (1.32%)	0 / 37 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 74 (0.00%)	1 / 76 (1.32%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			

subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	CSJ117 1mg	CSJ117 0.5mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	1 / 75 (1.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	CSJ117 8mg	CSJ117 4mg	CSJ117 2mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 74 (31.08%)	31 / 76 (40.79%)	20 / 37 (54.05%)
Vascular disorders			

Hypertensive crisis			
subjects affected / exposed	0 / 74 (0.00%)	1 / 76 (1.32%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	1 / 74 (1.35%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Vaccination site swelling			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Intermenstrual bleeding			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Asthma			
subjects affected / exposed	7 / 74 (9.46%)	12 / 76 (15.79%)	6 / 37 (16.22%)
occurrences (all)	4	9	4
Chronic rhinosinusitis with nasal polyps			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	3 / 74 (4.05%)	1 / 76 (1.32%)	0 / 37 (0.00%)
occurrences (all)	2	1	0
Rhinorrhoea			
subjects affected / exposed	1 / 74 (1.35%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			

subjects affected / exposed	0 / 74 (0.00%)	1 / 76 (1.32%)	1 / 37 (2.70%)
occurrences (all)	0	1	1
Nasal polyps			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Bronchial hyperreactivity			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood glucose increased			
subjects affected / exposed	0 / 74 (0.00%)	1 / 76 (1.32%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Vaccination complication			
subjects affected / exposed	0 / 74 (0.00%)	1 / 76 (1.32%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Cervicobrachial syndrome			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Spinal cord herniation			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Migraine			
subjects affected / exposed	0 / 74 (0.00%)	1 / 76 (1.32%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Headache			

subjects affected / exposed	1 / 74 (1.35%)	1 / 76 (1.32%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Splenomegaly			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 74 (0.00%)	1 / 76 (1.32%)	2 / 37 (5.41%)
occurrences (all)	0	1	1
Nausea			
subjects affected / exposed	2 / 74 (2.70%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	2	0	0
Dry mouth			
subjects affected / exposed	2 / 74 (2.70%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	2	0	0
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Cholelithiasis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Eczema			
subjects affected / exposed	0 / 74 (0.00%)	1 / 76 (1.32%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Pollakiuria			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	1 / 74 (1.35%)	2 / 76 (2.63%)	1 / 37 (2.70%)
occurrences (all)	1	2	1
Muscle tightness			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Spinal osteoarthritis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Acarodermatitis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Acute sinusitis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2

Candida infection			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
COVID-19			
subjects affected / exposed	1 / 74 (1.35%)	3 / 76 (3.95%)	0 / 37 (0.00%)
occurrences (all)	1	1	0
Bronchitis			
subjects affected / exposed	1 / 74 (1.35%)	1 / 76 (1.32%)	1 / 37 (2.70%)
occurrences (all)	1	1	1
Conjunctivitis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	0 / 74 (0.00%)	3 / 76 (3.95%)	3 / 37 (8.11%)
occurrences (all)	0	3	4
Gastroenteritis			
subjects affected / exposed	1 / 74 (1.35%)	1 / 76 (1.32%)	1 / 37 (2.70%)
occurrences (all)	0	1	1
Nasopharyngitis			
subjects affected / exposed	2 / 74 (2.70%)	4 / 76 (5.26%)	1 / 37 (2.70%)
occurrences (all)	2	1	1
Pharyngitis			
subjects affected / exposed	2 / 74 (2.70%)	2 / 76 (2.63%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Papilloma viral infection			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	1 / 74 (1.35%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	3 / 74 (4.05%)	1 / 76 (1.32%)	2 / 37 (5.41%)
occurrences (all)	3	1	2
Urinary tract infection			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0

Vaginal infection			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 74 (2.70%)	2 / 76 (2.63%)	0 / 37 (0.00%)
occurrences (all)	2	1	0
Laryngitis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 74 (1.35%)	1 / 76 (1.32%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Tracheitis			
subjects affected / exposed	0 / 74 (0.00%)	1 / 76 (1.32%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Pharyngitis bacterial			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	0
Otitis media acute			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	0
Oral fungal infection			
subjects affected / exposed	1 / 74 (1.35%)	0 / 76 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 76 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	0

Non-serious adverse events	CSJ117 1mg	CSJ117 0.5mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 37 (37.84%)	12 / 36 (33.33%)	27 / 75 (36.00%)
Vascular disorders			

Hypertensive crisis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	2 / 37 (5.41%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			
Vaccination site swelling			
subjects affected / exposed	1 / 37 (2.70%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	1 / 75 (1.33%)
occurrences (all)	0	1	1
Reproductive system and breast disorders			
Intermenstrual bleeding			
subjects affected / exposed	1 / 37 (2.70%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	2 / 75 (2.67%)
occurrences (all)	0	0	2
Asthma			
subjects affected / exposed	4 / 37 (10.81%)	2 / 36 (5.56%)	10 / 75 (13.33%)
occurrences (all)	4	2	9
Chronic rhinosinusitis with nasal polyps			
subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 37 (2.70%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			

subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Nasal polyps			
subjects affected / exposed	1 / 37 (2.70%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	0 / 75 (0.00%)
occurrences (all)	0	1	0
Bronchial hyperreactivity			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood glucose increased			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	1 / 75 (1.33%)
occurrences (all)	0	2	1
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	1 / 75 (1.33%)
occurrences (all)	0	1	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 37 (2.70%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Vaccination complication			
subjects affected / exposed	2 / 37 (5.41%)	0 / 36 (0.00%)	1 / 75 (1.33%)
occurrences (all)	2	0	4
Nervous system disorders			
Cervicobrachial syndrome			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	0 / 75 (0.00%)
occurrences (all)	0	1	0
Spinal cord herniation			
subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	0 / 75 (0.00%)
occurrences (all)	0	2	0
Headache			

subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	2 / 75 (2.67%)
occurrences (all)	0	1	2
Dysgeusia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	0 / 75 (0.00%)
occurrences (all)	0	1	0
Anaemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	0 / 75 (0.00%)
occurrences (all)	0	1	0
Splenomegaly			
subjects affected / exposed	1 / 37 (2.70%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	0 / 75 (0.00%)
occurrences (all)	0	1	0
Cholelithiasis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Eczema			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	0 / 75 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	1 / 37 (2.70%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	0 / 75 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	0 / 75 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	1 / 75 (1.33%)
occurrences (all)	0	1	1
Back pain			
subjects affected / exposed	1 / 37 (2.70%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Muscle tightness			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	0 / 75 (0.00%)
occurrences (all)	0	1	0
Spinal osteoarthritis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Acarodermatitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	0 / 75 (0.00%)
occurrences (all)	0	1	0
Acute sinusitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	1 / 75 (1.33%)
occurrences (all)	0	1	1

Candida infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	2 / 37 (5.41%)	4 / 36 (11.11%)	7 / 75 (9.33%)
occurrences (all)	0	5	4
Bronchitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	2 / 37 (5.41%)	2 / 36 (5.56%)	4 / 75 (5.33%)
occurrences (all)	1	2	5
Pharyngitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 36 (0.00%)	2 / 75 (2.67%)
occurrences (all)	1	0	1
Papilloma viral infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	0 / 75 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	1 / 37 (2.70%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	2	0	0
Sinusitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	2 / 75 (2.67%)
occurrences (all)	0	1	1
Urinary tract infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	0 / 75 (0.00%)
occurrences (all)	0	2	0

Vaginal infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	0 / 75 (0.00%)
occurrences (all)	0	1	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	1 / 75 (1.33%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	1 / 75 (1.33%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Tracheitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Pharyngitis bacterial			
subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Otitis media acute			
subjects affected / exposed	0 / 37 (0.00%)	1 / 36 (2.78%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Oral fungal infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 36 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 March 2020	The protocol was amended to allow inclusion of patients with absolute FEV1 variance at the end of run-in compared to the run-in visit <15% FEV1 predicted and exclude patients treated with a fixed dose combination of low dose fluticasone furoate and vilanterol, i.e., 92/22 µg o.d. or 100/25 µg o.d., as well as to prohibit re-screening of patients who failed during the run-in period.
22 January 2021	The protocol was amended to allow for optional off-site visits in place of clinic visits in selected countries and general public health emergency mitigation language. Assessment of the risks and benefits had not been impacted in the context of Covid-19. Modifications were also made to spirometry criteria to assist recruitment.
21 January 2022	The protocol was amended to provide an option of reducing the sample size based on a blinded sample size re-estimation that was to be conducted by assessing standard deviation for pre-dose FEV1 after approximately 150 subjects in the high eosinophil stratum had completed Week 8. The protocol was also amended to remove the requirement that patients must have had at least 1 prior asthma exacerbation in order to be eligible for inclusion in the study. By removing this criterion, it allowed for a broader range of patients who could benefit from a biologic, while still targeting a patient population who were symptomatic and in need of additional treatment. It was not anticipated based on prior data that the primary endpoint was impacted by the removal of this inclusion criterion.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported